REMARKS

Claims 1-4, 6-12 and 14-31 are pending in the present application. Claims 5 and 13 were previously cancelled. Claims 1-3, 8-11, 14 and 16 have been currently amended. New claims 17-31 have been added. Support for the amended and new claims can be found throughout the specification and in the original claims, and in particular, on the following pages of the specification. Support for amended Claims 1 and 9 can be found on pages 1-10 and 21-30. Support for amended Claims 2 , 3, 10 and 11 can be found on pages 14-15. Support for amended Claims 8, 16 and new Claim 26 can be found on page 20. Support for amended Claim 14 can be found on page 13 of the specification. Support for new Claims 17, 20 and 28 can found on pages 1-5 and 21-30. Support for new Claim 18 can be found on pages 10-13. Support for new Claims 19 and 27 can be found on pages 6-9, 13-14 and 20-30. Support for new Claims 21 and 29 can be found on pages 2-3, 13-15, 20, 23-24 and 28-30. Support for new Claims 22 and 30 can be found on pages 1-2, 6, and 20-22. Support for new Claim 24 can be found on pages 6, 9 and 21. Support for new Claim 25 can be found on pages 6-9, 13-14, 20, 22-25, 27 and 29-30. Support for new Claims 23 and 31 can be found on pages 22-23 of the specification.

No new matter has been added to the amended or new claims. Applicants respectfully request reconsideration of the present claims in view of the foregoing amendments and following remarks.

Compliance with Sequence Listing Rules

Applicants respectfully submit that a Sequence Listing for the nucleotide sequence provided on page 21, line 30 of the specification is enclosed with this response in accordance with 37 C.F.R 1.821-1.825.

Obviousness-Type Double Patenting Rejection

The Examiner rejected pending Claims 1-4, 6-12 and 14-16 under the judicially created doctrine of obviousness-type double patenting, as unpatentable over Claims 1, 5 and 9 of U.S. Patent 5,567,859 (hereinafter the '859 patent).

The Examiner found that although the conflicting claims are not identical, they are not patentably distinct from each other because the issued claims are drawn to polyoxyethylene/polyoxypropylene (POE/POP) copolymers that are similar in POP molecular weight and POE content to that claimed in the present application. The Examiner also asserted that, since the issued claims are drawn to compositions comprising copolymers of the recited characteristics, it is proper to look to the specification to examine what else is fairly suggested to be included in the invention; i.e., to examine the portions of the disclosure of the '859 patent which support its claims. The Examiner found that the '859 specification teaches the use of 2% Tween 80 and 1% ethanol, that the copolymers can be used in an admixture with a compound capable of altering gene expression and/or protein translation, and that the compositions are intended to be used for the delivery of nucleic acids to animals. Applicants respectfully traverse this rejection for the following reasons.

In an obviousness-type double patenting rejection, there must be clear evidence to establish why the invention's variation in a second patent or application would have been obvious. See *In re Kaplan*, 229 U.S.P.Q. 678, 683 (Fed. Cir. 1986). In addition, double patenting is based on whether the claims of a patent and application are directed to different, independent and distinct inventions. Inventions are independent and distinct, although they relate to the same basic process and are capable of cojoint use. See *In re Sutherland*, 146 U.S.P.Q. 485, 491 (C.C.P.A. 1965).

Claims 1, 5 and 9 of the '859 patent are directed to polyoxypropylene/polyoxyethylene block copolymers, **not** copolymer compositions or methods of delivering compounds using copolymer compositions. The claims in the present application are directed to novel copolymer compositions and methods of delivering a molecule using these novel copolymer compositions. The claims of the present application clearly show that independent and distinct inventions are involved; the present claims are directed to compositions and methods of delivery, and not to copolymers. The fact that the copolymers are capable of joint use does not negate the fact that the respective inventions are independent and distinct. Moreover, patentable subject matter exists for novel compositions and novel methods of use.

Furthermore, only the **claims** are compared in a double patenting rejection. See *Quad Environmental Technologies Corp. v. Union Sanitary District*, 20 U.S.P.Q.2d 1392, 1394 (Fed. Cir. 1991). Only copolymers are claimed in the '859 patent, thus only the disclosure of the '859 written description that is directed to the copolymers themselves should be used to support the issued claims and thus the double patenting rejection.

In addition, Applicants respectfully submit that the test for obviousness-type double patenting is whether the claimed invention in the subject application would have been obvious from the subject matter of the claims in the other case **in light of the prior art**. See *In re Longi*, 225 U.S.P.Q. 645, 648 (Fed. Cir. 1985). A patent's disclosure that fails to predate similar subject matter in the present application is not "**prior art**." The '859 patent (U.S. Patent Application Serial No. 08/292,803), is a continuation-in-part of a parent application, U.S. Patent Application Serial No. 08/087,136 (issued as Patent No. 5,523,492, now Patent No. Re. 36,665). The subject matter of the '859 patent relating to antisense oligonucleotides, triplex DNA compounds, ribozymes and other compounds capable of altering nucleic acid sequence function (found in Column 1, lines 60 - Column 2, lines 6 of the specification) was added to the continuation-in-part application upon filing, and was **not** present in the parent application. Therefore, the date for purposes of disclosure directed to antisense oligonucleotides, triplex DNA compounds, ribozymes, etc., in the '859 patent, should be the filing date of the '859 patent, which is August 9, 1994. The corresponding priority date for the present application is October 15, 1993, which predates the filing date of the '859 patent. Therefore, this subject matter disclosed in the '859 patent should not be used as prior art to support an obviousness-type double patenting rejection.

Therefore, for at least the above reasons Applicants respectfully request the withdrawal of the double-patenting rejection.

Rejection of Claims 1-4, 6-12 and 14-16 under 35 U.S.C. §112, First Paragraph (Enablement)

The Examiner rejected Claims 1-4, 6-12 and 14-16 under 35 U.S.C. §112, first paragraph, as lacking enablement. Applicants respectfully traverse this rejection for the following reasons.

Applicants respectfully submit that the law does not necessarily limit the claim scope only to those embodiments actually disclosed in the specification. In principle, one can support broad claims without a single disclosed embodiment. See *Spectra-Physics Inc. v. Coherent Inc., 827 F.2d 1524, 3 U.S.P.Q.2d 1737 (Fed. Cir. 1987).* Moreover, the specification may contain a written description of a broadly claimed invention without describing all species encompassed by the claim. See *Utter v. Hiraga, 845 F.2d 993, 998, 6 U.S.P.Q.2d 1709, 1714 (Fed. Cir. 1988).* Also, an embodiment need not necessarily been reduced to practice. See *In re Wright, 999 F.2d 1557, 1561, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993) ("Nothing more than objective enablement is required, and therefore it is irrelevant whether a teaching is provided through broad terminology or illustrated examples.")* Also, "the absence of a working example does not in and of itself compel the conclusion that a specification does not satisfy the requirements of section 112." *In re Long, 368 F.2d 892, 895, 151 U.S.P.Q. 640, 642 (C.C.P.A. 1966).*

The present specification provides numerous examples of compositions containing the polyoxyethylene/polyoxypropylene (POE/POP) and molecules of the pending claims. The specification also provides for the preparation of these compositions. For instance, Example 1 on page 21 of the specification provides a general preparation of compositions containing nonionic block copolymers with a variety of compounds capable of altering nucleic acid sequence. In this preparation, a compound capable of altering gene function is added to a copolymer (CRL-8131)/0.9% NaCl mixture that is solubilized at a temperature of 2-4°C. (See also page 19, lines 17-25: CRL-8131 can be used at a concentration of approximately 3% to 5%, however, copolymers that are more hydrophilic than CRL-8131 normally require a higher concentration (approximately 5-10%) of the copolymer.) Example 1 also describes a representative preparation of a composition containing CRL-8131 and an antisense oligonucleotide. Example 1 provides that a general effective amount of the antisense compound will result in a blood concentration of 1 μM to 100 μM, and that 6 mM to 600 mM of an oligonucleotide concentration is required when 1 ml injections are administered to an average person containing 6.25 liters of blood.

Example 3 on page 22 of the specification provides that a gene therapy composition may be prepared by combining a copolymer, such as CRL-8131, with a normal copy of a

defective gene, such as a normal copy of the adenosine deaminase gene. Example 6 on page 23 of the specification provides that a composition comprising the CRL-8131 copolymer and the expression vector containing the gD gene of *Herpes simplex* virus type-1 was used for an actual transfection experiment. Applicant's specification provides numerous other examples of block copolymer compositions. These examples include, but are not limited to, Example 8 (five different compositions prepared from DNA and CRL 1122, 3362, 3632, 9352 and 8131); Example 9 (six different compositions prepared from DNA and copolymers 1183, 1187, 8131, 1235, 8950AQ and 1190AQ); Example 10 (compositions prepared from different copolymer solutions and β-galactosidase encoding DNA); Example 12 (a composition was prepared from copolymer 1029 and a cDNA encoding the hemagglutinin-esterase (HE) glycoprotein of bovine coronavirus (pCDNA/HE)); and Example 13 (compositions prepared from a plasmid pCDNA carrying a DNA fragment encoding the gB or gD genes of the *Herpes simplex* virus (HSV) with copolymer 1029 and 1190). Descriptive text of compositions of the present invention are found throughout the specification, including, but not limited to, page 6, lines 5-28; page 7, line 1-18; page 9, lines 5-24; page 10, line 17 to page 11, line 3; pages 13-15 and page 20.

Applicants also respectively submit that the specification provides numerous examples of methods of delivering a compound to an animal; comprising administering to the animal a composition comprising the polyoxyethylene/polyoxypropylene (POE/POP) and molecules of the pending claims ("animal" refers to both humans and animals). For instance, Example 2 on page 22 provides that an antisense oligonucleotide/CRL-8131 composition of Example 1 can be administered to HIV patients by any route effective to reduce viral activity; the preferred route being intravenous injection. Moreover, the compositions of the present invention can be administered by a number of routes including, but not limited to, topical, transdermal, oral, trans-mucosal, subcutaneous injection, intravenous injection, interperitoneal injection and intramuscular injection (see page 6, lines 29-33). Example 3 provides that a composition containing a normal copy of a defective gene (eg. normal copy of the adenosine deaminase gene (ADA)), and the CRL-8131 copolymer is transfected with blood from a human or animal, and then the transfected blood is reintroduced into the respective animal or human. Example 4 provides that the composition of Example 3 is combined with isolated T-

lymphocytes, to form T-lymphocytes containing the ADA gene, and then subsequently administered into a patient suffering from adenosine deaminase deficiency. Example 5 provides that compositions similar to those in Examples 3 and 4 can be used as a DNA vaccine-induced immunization. Example 7 provides a DNA-induced immunization in rabbits. Example 12 provides for the inoculation of mice with DNA (cDNA encoding the hemagglutinin-esterase (HE) glycoprotein of the bovine coronavirus) in combination of copolymers of the present invention. Also, Example 13 provides for the inoculation of mice with plasmid cDNA carrying the DNA fragment encoding the gB or gD genes of *Herpes simplex* virus (HSV), together with copolymer 1029 or 1190. Descriptive text of Applicants' claimed methods of delivery can also be found throughout the specification, including, but not limited to, pages 5-8, 15 and 20.

Applicants also submit that the specification provides enablement for methods of delivering a compound for altering gene activity and associated compositions. For instance, in Example 13, compositions comprising block copolymer 1029 or 1190 and plasmids bearing the gB or the gD genes of *Herpes simplex* virus delivered the gB or gD genes to mice. These genes were expressed as proteins, and antibodies directed to the virus were generated. (See also Example 7 for the DNA-induced immunization in rabbits). Similarly, a cDNA encoding the hemagglutinin-esterase glycoprotein of bovine coronavirus was expressed in mice to give the encoded product after co-administration of the cDNA and copolymer 1029. Details of the procedure are presented in Example 12. Example 1 provides that one skilled in the art can readily test the relative effectiveness of any particular antisense oligonucleotide according to the *in vivo* test of Matsukura *et al.* (see page 21, lines 22-26 and page 22, lines 7-9). Thus, compositions containing antisense oligonucleotides can be evaluated according to this test. In addition, throughout the present specification, support for methods of delivering a compound for altering gene activity, is provided, including, but not limited to, the following pages: 6-9, 13-14 and 20-30.

Therefore, for at least the above reasons, Applicants respectfully submit that Claims 1-4, 6-12 and 14-16 are enabled by the present specification. Accordingly, Applicants request the withdrawal of this rejection.

Rejection of Claims 1-4, 6-12 and 14-16 under 35 U.S.C. §112, First Paragraph (Written Description)

The Examiner rejected Claims 1-4, 6-12 and 14-16 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art, that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection for the following reasons.

An adequate written description of the claimed invention may be shown by any description of sufficient, relevant, identifying characteristics, so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. MPEP 2163. Moreover, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species ..., or by disclosure of relevant identifying characteristics ..., by functional characteristics coupled with known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP 2163. The present specification provides sufficient description of the terms "genes," "oligonucleotides," "antisense oligonucleotides," "triplex DNA compounds" and "ribozymes," by using identifying characteristics, functional characteristics and/or descriptive representations. For example, the term "genes" is defined by relevant identifying characteristics and functional characteristics on the following pages of the specification: page 3, lines 11-12 (genes that code for therapeutic compounds); page 13, lines 35-36 (gene that code for the gene product to be immunized against); and page 14, lines 4-5 (genes that code for compounds effective for killing, reducing or retarding cancer). "Oligonucleotides" are defined in term of relevant identifying characteristics and functional characteristics on the following pages of the specification: page 1, lines 34-35 (oligonucleotides that are complimentary to certain gene messages or viral sequences); and page 3, lines 33-35 (oligonucleotides that specifically bind to particular regions of duplex DNA, thereby inactivating the target gene). "Antisense oligonucleotides" are defined in term of relevant identifying characteristics and functional characteristics on the following pages of the specification: page 1, lines 33-35 (oligonucleotides that are complimentary to certain gene

messages or viral sequences); and page 20, lines 7-8 (antisense oligonucleotides use for altering or regulating gene expression and/or protein translation). "Triplex DNA compounds" are defined in term of relevant identifying characteristics and functional characteristics on the following pages of the specification: page 3, lines 33-35 (triplex DNA compounds specifically bind to particular regions of duplex DNA to inactivate the target gene). "Ribozymes" are defined in term of relevant identifying characteristics and functional characteristics on page 4, lines 10-17 of the specification (ribozymes are catalytic RNA molecules that consist of a hybridizing region and an enzymatic region).

Applicants also submit that representative examples of "genes" are found on pages 22, 24, 27-28 and 30 of the specification (adenosine deaminase gene, gD gene of *Herpes simplex* virus type-1, β-galactosidase encoding DNA, cDNA encoding the hemagglutinin-esterase (HE) glycoprotein of bovine coronavirus and plasmid cDNA carrying a DNA fragment encoding the gB or gD genes of the *Herpes simplex* virus (HSV)). Representative examples of antisense oligonucleotides are found on page 21, lines 22-26 and lines 27-31 of the specification (antisense oligonucleotides sequence, such as those disclosed by Matsukara *et al.* are incorporate by reference; a sequence complimentary to regions of the *art/trs* genes of HIV are prepared according to the method of Matsukara). Also, as stated above, the present specification describes numerous examples of compositions containing the polyoxyethylene/polyoxypropylene (POE/POP) and molecules of the pending claims. Examples 1, 3, 6, 8-10, and 13 of the present specification describe several examples of these compositions. Additional descriptions of these compositions are found throughout the specification including, but not limited to, pages 6-7, 9-11, 13-15 and page 20 of the specification.

For at least the above reasons, Applicants respectfully submit that Claims 1-4, 6-12 and 14-16 are sufficiently described in the specification as to reasonable convey to one skilled in the art, that the Applicants, at the time the present application was filed, had possession of the claimed invention. Accordingly, Applicants request the withdrawal of this rejection.

Rejection of Claims 1-4, 6-12 and 14-16 under 35 U.S.C. §112, Second Paragraph

The Examiner rejected Claims 1-4, 6-12 and 14-16 under 35 U.S.C. §112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter, which Applicants regard as the invention. The Examiner asserted that Claims 1-4, 6-12 and 14-16 were unclear as to the meaning of the term "genes." The Examiner also asserted that Claim 8 lacked antecedent basis, and that Claims 14-16 were unclear as to how the addition of a surfactant, alcohol or expression vector further limited these method claims. Applicants respectfully traverse this rejection for the following reasons.

Applicants have amended Clams 1 and 9 to recite "isolated or amplified nucleic acid sequences encoding gene products." Applicants respectfully submit that this phrase refers to any gene-encoding sequence, and thus refers to both open reading frame sequences and those sequences adjacent to, or including, one or more noncoding sequences. Applicants have also amended Claim 8 to provide a proper antecedent basis for this claim, and have amended Claims 14 and 16 to recite that the compositions further comprise the respective additional components. Therefore, for at least the above reasons, Applicants respectfully assert that Claims 1-4, 6-12 and 14-16 are definite, and request the withdrawal of this rejection.

Rejection of Claims 1-4 and 9-12 under 35 U.S.C. §102(e)

The Examiner rejected Claims 1-4 and 9-12 under 35 U.S.C. §102(e), as anticipated by either U.S. Patent 5,376,369, to Allison et al. (hereinafter "Allison"), or U.S. Patent 5,656,275 to Wasmoen et al. (hereinafter "Wasmoen"). The Examiner found that Allison taught that Pluronics L101, L121 and L122 could be used as adjuvants in the delivery of whole viruses as vaccines. The Examiner further found that Wasmoen taught that Pluronics L121 could be used as an adjuvant in the delivery of whole viruses. The Examiner noted that whole viruses comprise nucleic acids encoding genes, and can be considered expression vectors. The Examiner also noted that the compositions and method in these references do not require the function of viral nucleic acids for vaccine activity; rather this activity depends on protein antigens in the viruses. Applicants respectfully traverse this rejection for the following reasons.

Claims 1 is directed to a composition comprising a nonionic block copolymer and one or more molecules selected from isolated or amplified nucleic acid sequences encoding gene products, oligonucleotides, antisense oligonucleotides, triplex DNA compounds, ribozymes, or mixtures thereof. Claim 9 is directed to a method of delivering a molecule to an animal, comprising administering to the animal the composition of Claim 1. Applicants respectfully submit that neither Allison nor Wasmoen teach or suggest the compositions, and thus methods, of Applicants' claimed invention. Allison and Wasmoen fail to teach or suggest isolated or amplified nucleic acid sequences encoding gene products, oligonucleotides, antisense oligonucleotides, triplex DNA compounds, ribozymes, or mixtures thereof. Allison and Wasmoen teach whole viruses for use as vaccines, but do not teach or suggest isolated or amplified nucleic acid encoding genes in combination with the claimed block copolymers.

Applicants note that newly Claim 25 specifies that the method delivers the molecule **into a cell**. Neither Allison nor Wasmoen teach delivery into a cell as claimed.

Therefore, for at least the above reasons, Applicants respectfully submit that neither Allison nor Wasmoen teach or suggest Claim 1 or Claim 9. Since Claims 2-4, 6-8, and 10-12 respectively depend, directly or indirectly, from either Claim 1 or Claim 9, Applicants respectfully submit that the above references do not teach or suggest these dependent claims. Accordingly, Applicants respectfully request the withdrawal of this rejection.

CONCLUSION

Claims 1-4, 6-12 and 14-31 are pending in the present application. Claims 5 and 13 were previously cancelled. Claims 1-3, 8-11, 14 and 16 have been currently amended. New Claims 17-31 have been added. For at least the reasons given above, Applicants respectfully submit that the pending claims define patentable subject matter. Accordingly, Applicants respectfully request allowance of these claims.

A check in the amount of $465.00, the fee for a three-month extension of time, is enclosed. Also enclosed is a check in the amount of $123.00, the fee for nine additional claims (one independent claim and eight dependent claims). No additional fees are believed due; however, the Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, to Deposit Account No. 11-0855.

Applicants submit that the claims in the present application are in condition for allowance, and such action is courteously solicited. The Examiner is invited and encouraged to contact the undersigned attorney of record at telephone number listed below, if such contact will facilitate an efficient examination and allowance of the application.

Respectfully submitted,

Jane M. Terry

Jane M. Terry
Reg. No. 53,682

KILPATRICK STOCKTON LLP
1100 Peachtree Street, Suite 2800
Atlanta, Georgia 30309
Telephone: 404-815-6500
Our Docket No.: 19720-0624 (42896-216422)